together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2(aryl)$, $-CH(aryl)OH$, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH(aryl)$, $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom, with the proviso that M-PO_3^{2-} is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable salts of Formula I;

and a pharmaceutically acceptable excipient.

2 169. (Previously Amended) The pharmaceutical composition of claim 1 168, wherein MH is 9-(2-phosphonylmethoxyethyl)adenine (PMEA) or analogues thereof.

7 cont - 3 170. (Previously Amended) The pharmaceutical composition of claim 1 168, wherein MH is 9-(2-phosphonylmethoxyethyl)adenine (PMEA).

4 171. (Previously Amended) The pharmaceutical composition of claim 1 168, wherein MH is selected from penciclovir, 3TC, ACV, PMPA, araC, ribavirin, fludarabine, and 5-fluoro-2'-deoxyuridine.

5 172. (Previously Amended) The pharmaceutical composition of claim 1 168, wherein MH is radiolabelled 2'-deoxy-5-Iodouridine.

6 173. (Previously Amended) The pharmaceutical composition of claim 5 172 wherein MH is 2'-deoxy-5-^{131}I-iodouridine.

7 174. (Previously Amended) The pharmaceutical composition of claim 1 168, wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

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175. (Previously Amended) The pharmaceutical composition of claim 168, wherein the prodrug is in the *cis* configuration.

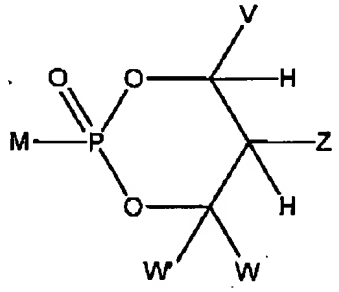
176. (Previously Amended) The pharmaceutical composition of claim 174, wherein the prodrug is in the *cis* configuration.

177. (Previously Amended) The pharmaceutical composition of Claim 171, wherein MH is araC and V is a heteroaryl group.

178. (Previously Amended) The pharmaceutical composition of claim 177, wherein V is 4-pyridyl.

179. (Previously Amended) The pharmaceutical composition of claim 172 wherein MH is 2'-deoxy-5-^{125}I-iodouridine.

180. (Previously added) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group consisting of hydrogen, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and

1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein the cyclic group optionally contains one heteroatom and is substituted with a hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy group attached to a carbon atom that is three atoms away from both oxygen atoms that are attached to the phosphorus atom; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$(aryl), $-CH$(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH$(aryl), $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

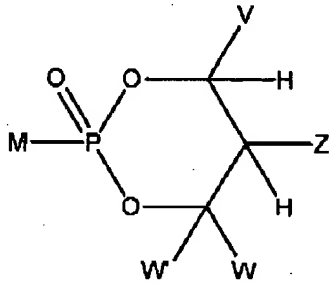
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon atom, with the proviso that MPO_3^{2-} is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

181. (Previously added) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group consisting of hydrogen, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein the cyclic group optionally contains one heteroatom and is substituted with a hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy group attached

to a carbon atom that is three atoms away from both oxygen atoms that are attached to the phosphorus atom; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2(aryl)$, $-CH(aryl)OH$, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH(aryl)$, $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

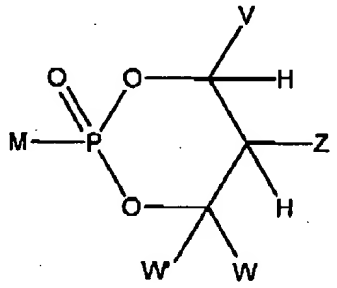
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via an oxygen atom, with the proviso that MPO_3^{2-} is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

182. (Previously added) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group consisting of hydrogen, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein the cyclic group optionally contains one heteroatom and is substituted with a hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy group attached to a carbon atom that is three atoms away from both oxygen atoms that are attached to the phosphorus atom; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group wherein the cyclic group optionally contains one heteroatom, and is fused to an aryl group, at the beta and gamma position to the oxygen attached to the phosphorus; or

together V and W are connected via an additional three carbon atoms to form an optionally substituted cyclic group containing six carbon atoms and is optionally substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy groups, wherein such substituent is attached to one of said carbon atoms that is three atoms away from an oxygen attached to the phosphorus atom; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2(aryl)$, $-CH(aryl)OH$, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH(aryl)$, $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$;

R^2 is selected from the group consisting of R^3 and hydrogen;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

p is an interger 2 or 3;

with the provisos that:

a) V, Z, W, and W' are not all hydrogen; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not hydrogen, alkyl, aralkyl, or alicyclic; and

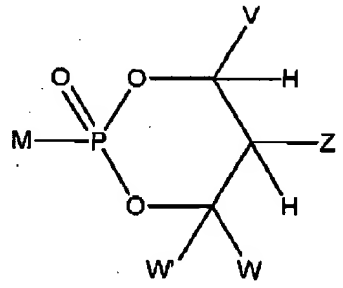
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a nitrogen atom, with the proviso that MPO_3^{2-} is not an FBPase inhibitor;

wherein said compound of Formula I is converted to MPO_3H_2 by human liver microsomes;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

183. (Currently amended) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

W and W' are independently selected from the group of H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkynyl and 1-alkenyl;

Z is selected from $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2(aryl)$, $-CH(aryl)OH$, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OC(O)R^3$, $-OCO_2R^3$, $-SC(O)R^3$, $-SCO_2R^3$, $-NHC(O)R^2$, $-NHCO_2R^3$, $-CH_2NH(aryl)$, $-(CH_2)_pOR^{12}$, and $-(CH_2)_pSR^{12}$; or

together V and Z are connected via 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the oxygen attached to the phosphorus;

p is an integer 2 or 3;

R^2 is selected from the group of R^3 and –H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of hydrogen, and lower acyl; and

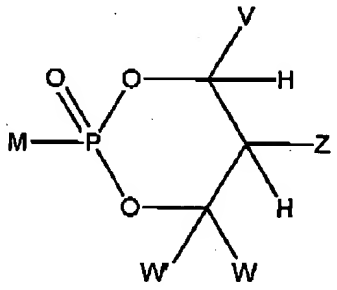
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom;

wherein said compound of formula I is converted to MPO_3H_2 by human liver microsomes, with the proviso that $M\text{-}PO_3^{2-}$ is not an FBPase inhibitor;

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

184. (Currently amended) A pharmaceutical composition comprising a compound of Formula I:



Formula I

wherein:

V, W and W' are independently selected from the group of –H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

Z is selected from the group of: $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OCO_2R^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OC(S)OR^3$, –CH(aryl)OH, $-CH(CH=CR^2{}_2)OH$, $-CH(C\equiv CR^2)OH$, $-SR^2$, $-CH_2NHaryl$, $-CH_2$ aryl; or

together V and Z are connected via 3-5 carbon atoms to form a cyclic group, optionally containing heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from an oxygen attached to phosphorus;

R^2 is selected from the group of R^3 and H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl; and

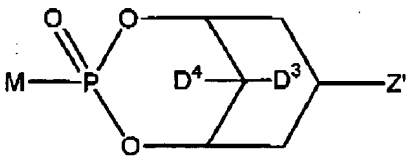
M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom;

wherein said compound of formula I is converted to MPO_3H_2 by human liver microsomes, with the proviso that $M\text{-}PO_3^{2-}$ is not an FBPase inhibitor

pharmaceutically acceptable prodrugs and salts of Formula I;

and a pharmaceutically acceptable excipient.

185. (Currently amended) A pharmaceutical composition comprising a compound of Formula VIII:



VIII

wherein:

Z' is selected from the group of –OH, $-OC(O)R^3$, $-OCO_2R^3$, and $-OC(O)SR^3$;

D^4 and D^3 are independently selected from the group of –H, alkyl, $-OR^2$, –OH, and $-OC(O)R^3$; with the proviso that at least one of D^4 and D^3 are –H;

R^2 is selected from the group of R^3 and H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl; and

M is selected from the group that, attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$, is biologically active *in vivo* and that is attached to the phosphorus atom in Formula I via a carbon, oxygen, or nitrogen atom;

wherein said compound of formula I is converted to MPO_3H_2 by human liver microsomes, with the proviso that $M\text{-}PO_3^{2-}$ is not an FBPase inhibitor;

and pharmaceutically acceptable prodrugs and salts of Formula VIII;

and a pharmaceutically acceptable excipient.

7, 1 cancel

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